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AMRL-TR-67-69

THE EFFECT OF A MIXED GAS ATMOSPHERE AT 5 PSIA ON THE INHALATION TOXICITY OF O_3 AND NO_2

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Aerojet-General Corporation

DECEMBER 1967

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AEROSPACE MEDICAL RESEARCH LABORATORIES
AEROSPACE MEDICAL DIVISION
AIR FORCE SYSTEMS COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

NOTICES

The experiments reported herein were conducted according to the "Principles of Laboratory Animal Care" established by the National Society for Medical Research.

600 - May 1968 - CO455 - 36-764

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FOREWORD

This is one of a series of technical reports describing results of the experimental laboratory program being conducted in the Toxic Hazards Research Unit. This report is concerned with the response of animals exposed to varying pressures of different atmospheres of ozone (O_3) and nitrogen dioxide (NO_2) for periods of 14 days. The experimental program has been accomplished by the Aerojet-General Corporation (Azusa, California) under Contract AF 33(657)-11305 for the Toxicology Branch, Toxic Hazards Division, Biomedical Laboratory, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio 45433. The contract was initiated in support of Project No. 6302, "Toxic Hazards of Propellants and Materials," and Task No. 630301, "Toxicology." K. C. Back, Ph. D., is the technical contract monitor for the Aerospace Medical Research Laboratories. The research described in this report was conducted during the period from October, 1964 through July, 1966.

J. D. MacEwen, Ph. D., is the Principal Investigator for the contractor in the conduct of the research program. Acknowledgement is made to N. M. Breene for assistance in the preparation of this report.

This report is identified as Aerojet-General Corporation Report No. 3267.

This technical report has been reviewed and is approved.

WAYNE H. McCANDLESS
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ABSTRACT

A mixed gas atmosphere (68% O_2-32% N_2) at 5 psia pressure was shown to reduce the acute toxic effect of ozone (O_3) in animals when compared with an identical O_3 concentration under ambient pressure conditions. The actual reduction of O_3 toxicity in the 5 psia-mixed gas environment was not as great as that seen in a 5 psia-100% O_2 environment. Further experimentation with increased O_2 partial pressures at ambient total pressures led to the conclusion that an increased pO_2 of 260 mm Hg was protective against acute O_3 effects. No significant differences were seen between 5 psia-mixed gas and 5 psia-100% O_2 environments on the effect of nitrogen dioxide (NO_2) toxicity in animals although both provide some apparent protection compared with ambient pressure conditions.

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SECTION I

INTRODUCTION

The advent of manned space flight has created a need for toxicity information involving environmental conditions not hitherto studied. Probably the most important of these are continuous exposure, reduced pressures, and higher than normal partial pressures of oxygen (O_2) in the breathing atmosphere.

Preliminary efforts in the study of continuous contaminant exposure were reported by Sandage (References 1 and 2) and by House (Reference 3). Welch and others (References 4 and 5) have described human responses to reduced pressure in 100% O_2 and mixed gas environments for periods up to 58 days. The first experiments combining these environmental conditions were reported by McNerney and MacEwen (Reference 6) in which three model compounds, ozone (O_3), nitrogen dioxide (NO_2), and carbon tetrachloride (CCl_4), were used to evaluate differences resulting from continuous contaminant exposures for two-week periods in 100% O_2 at 5 psia pressure and at ambient pressure in normal air. The primary conclusion drawn from these studies was that the 5 psia-100% O_2 environment produced a protective effect.

Recently, it was announced that the cabin environment of the Air Force Manned Orbiting Laboratory (MOL) would be composed of two gases, O_2 and helium (He), with a pO_2 of 175 mm Hg. The question arose whether the protective action against pulmonary irritants seen with a 5 psia-100% O_2 environment would extend to this lower O_2 partial pressure mixture. An experimental protocol, similar to that used previously for two-week continuous exposures to intermediate chamber concentrations of NO_2 and O_3 (38.8 and 8.0 mg/M^3, respectively), was designed to study the effect of mixed-gas environments on the toxicity of these gases. Nitrogen (N_2), rather than He, was used as the inert part of the gas mixture. The reason for its application is two-fold:

1) The chambers were already equipped to prepare air-oxygen mixtures and the desired mixture could be obtained by proper adjustment of the gas blending valves.

2) The use of He would have required modification of the chamber gas supply system and the costly installation of He storage facilities.

SECTION II

MATERIALS AND METHODS

CHAMBERS

Inhalation exposures were conducted in specially designed chambers known as Thomas Domes (Reference 7), capable of operating at pressures between 5 psia (258 mm Hg) and 14.7 psia (760 mm Hg). These chambers are equipped to operate with either 100% O_2, ambient air, or a mixture of these gases over a range of 20% to 100% O_2 in the atmosphere of the chamber. The chambers are completely automated to control temperatures at 72 ± 5 F and relative humidity at $50 \pm 10\%$. Gas flows through the chamber may be varied from 0 to 125 cfm, although normal animal exposure operations are conducted at 20 cfm. The chamber flow rate of 20 cfm is capable of maintaining carbon dioxide concentrations below 0.5% (with a normal operating range of 0.1 to 0.2%) when the chamber is fully loaded with animals.

Entry into the chambers was required for feeding and cleaning animals, as well as for removal of animals that died during the experiments. The chamber was provided with an air lock to effect entry into the chambers without disruption of the experimental environmental conditions. Before entering a chamber operating at reduced pressure and 100% O_2, technicians were denitrogenized by breathing O_2 for an hour. The chamber technician then entered the chamber air lock which was flushed with O_2 until all N_2 was removed, as measured by a paramagnetic O_2 sensor. When flushing of the air lock was completed, the depressurization phase was initiated. After the pressure was equilibrated between the air lock and the exposure chamber, a connecting hatchway was opened, and the technician entered the chamber to carry out his routine assignments. Since contaminant concentrations within the chamber exceeded the threshold limit values, the technician wore a face mask, and carried an independent O_2 supply.

When the experiments were conducted at ambient pressure in these chambers, entry was still effected through the air lock, and the technician was provided with a self-contained breathing apparatus for use while conducting his duties within the chamber.

Given below are the atmosphere compositions and pressures used in the experiments:

Total pressure (mm Hg)	700	260	260	720
pO_2(mm Hg)	140	175	260	260
Gas Supply	Air	68% O_2 32% N_2	100% O_2	36% O_2 64% N_2

ANIMALS

Four animal species were selected for these experiments in an attempt to observe species variation as well as differences which might result from the environmental conditions tested. These species were Macaca mulatta monkeys, beagle dogs, albino rats of the Sprague-Dawley strain, and mice of the Harlan ICR strain. Guinea pigs were also included in the O_3 experiments, since they were reported to be particularly susceptible to this contaminant.

A normal dome-loading consisted of 50 albino rats, 40 mice, 8 dogs, and 4 monkeys, all equally divided with respect to sex except the mice, which were all males. Other numbers of animals were sometimes used depending upon the number available. In some O_3 experiments, 8 male guinea pigs were used. Unexposed control animals for each experiment were maintained in another chamber. These controls were subjected to the same environmental conditions with the exception of the contaminant supplied to the test groups. Equal numbers of rats, mice, and guinea pigs were used as controls; the number of controls for dogs was 4, and for monkeys, 2. An additional group of control rats and mice was maintained in the animal colony to serve as a second type of control. All surviving animals were killed at the end of the 2-week exposure periods, and specimens were submitted for histopathologic examination.

OZONE

The O_3 used for animal exposures was produced from O_2 by electrical discharge in a high-voltage silent-discharge generator. An excess of O_3 was produced and a portion was metered in the chamber gas supply stream while the remainder was vented to a waste disposal system. O_3 concentrations were monitored by means of grab samples collected in a tonometer and analyzed by the method of Byers and Saltzman (Reference 8). Continuous O_3 analyses were also conducted using an O_3 meter which operates through a modified coulometric technique.

NITROGEN DIOXIDE

The desired NO_2 chamber concentrations were achieved by metering controlled amounts of a 1% NO_2 mixture into the gas supply duct of the exposure chamber. The 1% feed mixture was prepared by diluting cylinder NO_2 with either air or O_2 depending upon experimental conditions. The NO_2 cylinder with its associated valves and stainless steel plumbing was wrapped with heating tapes to maintain the gas phase and prevent condensation at valve points due to rapid adiabatic expansion when the exposure chambers were operated at reduced pressure (5 psia).

Chamber air samples were collected periodically in a tonometer, repressurized with dry O_2, and analyzed by the Saltzman method (Reference 9). The Saltzman sampling solution was introduced into the tonometer by a syringe through a rubber capped side arm and then brought in contact with the sampled NO_2 by shaking. Automatic continuous analysis was not performed until most of the individual experiments were completed due to technical difficulties involved with pressure differentials.

SECTION III

EXPERIMENTAL RESULTS

Summaries of data from individual experiments are presented in the Appendix. Detailed discussions of these data are presented in succeeding sections.

BASELINE DATA FOR MIXED-GAS ENVIRONMENT (68% O_2-32% N_2, 5 PSIA)

An experiment was conducted to verify that the mixed gas environment (32% N_2-68% O_2) at 5 psia pressure had no measurable biological effect during a 14-day exposure period; therefore, any effects seen in subsequent experiments conducted exposing animals to this contaminant, under these experimental conditions, would be clearly attributable to the contaminant.

Baseline values were obtained for two species (dogs and monkeys) in each of three groups consisting of animal room controls, dome test controls, and a third group of animals which was later used in an actual contaminant exposure. The baseline values represent 5 nonfasting preexposure determinations at 2-week intervals. For a period of 2 weeks, the dome test control group was then subjected to the same environmental conditions as the "test" group, but without the pulmonary irritant gas. At the end of that period, examination of the clinical laboratory test values of the dome control animals exposed to the mixed-gas environment at 5 psia showed no significant differences from their own preexposure values or the baseline and final values of the animal room controls. The values for the blood constituents studied in beagle dogs and monkeys are shown in Table I. Although there appears to be a slight upward trend in SGPT and SGOT levels, the increase is not significant and is within the normal variation of individual animals. Growth rates and organ-to-body weight ratios are comparable in both the animal room and dome test control animals.

OZONE EXPOSURES

The 14-day continuous exposure of laboratory animals to an O_3 chamber concentration of 8.0 mg/M^3 in the mixed-gas environment at 5 psia resulted in a lower mortality rate than that observed at ambient conditions and previously reported (Reference 10). The data from experiments relating to O_3 in Table I are summarized in Table III. There was no significant change in rodent mortality, but in dogs and monkeys an effect intermediate to those in ambient air and 5 psia-100% O_2 environments appeared to be in proportion to the O_2 partial pressure.

TABLE I
EFFECT OF 5 PSIA-MIXEDGAS ENVIRONMENT,
68% O_2 - 32% N_2 14-DAY CONTINUOUS EXPOSURE
ON CLINICAL LABORATORY TEST VALUES

BLOOD TEST	UNITS	BEAGLE DOGS			MONKEYS		
		BASE LINE	14 DAY EXPOSURE	A. R. CONTROLS	BASE LINE	14 DAY EXPOSURE	A. R. CONTROLS
HCT	(Vol. %)	44	44	49	40	43	41
HGB	(gm. %)	14.9	14.2	15.6	12.6	12.8	12.0
RBC	(x 10^6)	6.2	6.2	6.8	5.3	5.5	5.3
WBC	(x 10^3)	14.4	15.5	13.8	10.9	12.8	13.4
SODIUM	(mEq./l.)	143	143	148	145	144	148
POTASSIUM	(mEq./l.)	4.7	5.1	5.6	4.5	4.2	5.1
CALCIUM	(mEq./l.)	5.5	5.4	5.9	5.4	5.2	6.0
T. PROTEIN	(gm. %)	5.5	6.0	6.0	7.6	7.6	7.3
ALBUMIN	(gm. %)	3.3	3.3	3.6	4.6	4.6	3.9
SGPT	(U./ml)	24	31	21	31	35	20
SGOT	(U./ml)	29	36	37	42	49	38
ALK. P'TASE	(U./ml)	2.3	2.5	1.8	25	19	14
T. PHOS.	(mg. %)	5.4	6.1	6.0	5.1	6.1	4.4
LDH	(U./ml)	234	324	382	429	408	475

In order to verify the protective effect of O_2 against O_3 toxicity, 2 additional experiments were conducted at near ambient pressure (720 mm Hg) air enriched with oxygen to produce a pO_2 of 260 mm Hg. Only dogs and monkeys were used in the first experiment since there had been no clear cut protection in rodents during prior experiments. Four species were exposed during the second experiment with similar results. The mortality response was significantly reduced as shown in Table II. The clinical symptoms of O_3 toxicity that were observed in the exposed animals yielded results which were markedly reduced from those observed in animals exposed under the other 3 environmental conditions.

Clinical blood test data on samples taken from survivors showed no significant differences among the animals exposed to 8.0 mg/M^3 concentrations in the 4 environmental conditions studied. There were differences, however, in the lung weight to body weight ratios, shown in Table III, for the various test environments. The intermediate pO_2 of the mixed-gas environment resulted in the highest lung weight to body weight ratio while the 2 tests conducted at near ambient pressure with O_2 enriched air resulted in a near normal pattern.

NITROGEN DIOXIDE EXPOSURES

The effects of mixed-gas environments at reduced pressure on NO_2 toxicity were somewhat different from those seen in O_3 toxicity. As shown in Table IV, there appears to be an intermediate effect in monkey mortality in comparison with ambient and 5 psia-100% O_2 conditions. However, when dogs and monkeys were challenged with the same atmospheric concentrations of NO_2 in oxygen-enriched air at near ambient pressure, the toxic response was more like that seen earlier in air at near ambient pressure; i.e., no decrease in mortality. Again, rodents were not used since insignificant mortality had been observed in previous exposures at the same chamber concentration of toxicant.

There was some indication of prolongation of time to produce death in the near ambient pressure O_2-enriched experiment; therefore, another experiment was conducted challenging the animals to a higher concentration of NO_2 under the same environmental conditions. The results of this experiment are compared in Table V with previous studies of increased contaminant concentrations conducted in this laboratory. The O_2-enriched atmosphere did delay the time of death and the surviving animals showed clinical signs of improvement. The experiment was terminated after 5 days, however, since the information sought had already been obtained.

Clinical chemistry and hematology data obtained from survivors of the NO_2 exposures showed no significant differences from their controls (Appendix).

TABLE II
MORTALITY PRODUCED DURING
14-DAY CONTINUOUS EXPOSURE
TO OZONE - 8.0 mg/M^3
(NO. DEATHS/NO. EXPOSED)

TOTAL PRESSURE (mm Hg)	700	260	260	720	700
pO_2 (mm Hg)	140	175	260	260	260
GAS SUPPLY	Air	68% O_2 - 32% N_2	100% O_2	36% O_2 - 64% N_2	36% O_2 - 64% N_2
SPECIES					
MICE	33/40	32/40	33/40	-	16/40
RATS	50/50	45/50	45/50	-	15/50
GUINEA PIGS	8/8	9/9	8/8	-	-
DOGS	5/5	6/8	2/8	0/8	2/8
MONKEYS	2/4	1/4	0/4	0/4	0/9

TABLE III
EFFECT OF OZONE ON LUNG WEIGHT TO BODY WEIGHT RATIO
FOR A 14-DAY CONTINUOUS EXPOSURE

(CHAMBER CONCENTRATION - 8.0 mg/M^3)

TOTAL PRESSURE (mm Hg)	700	260	260	720	700	UNEXPOSED CONTROLS
pO_2 (mm Hg)	140	260	175	260	260	
GAS SUPPLY	Air	100% O_2	68% O_2 - 32% N_2	36% O_2 - 64% N_2	36% O_2 - 64% N_2	
BEAGLE DOGS						
MALES (4) TEST	.033	.029	.041	.019	.026	.012
FEMALES (4) TEST	.039	.020	.053	.018	.014	.010
MONKEYS						
MALES (2) TEST	.016	--	.021	.011	.012	.009
FEMALES (2) TEST	--	.010	.018	.012	.009	.007
RATS						
MALES (25) TEST	.026	.021	.024	--	.021	.006
FEMALES (25) TEST	.027	.025	.025	--	.019	.008

TABLE IV
MORTALITY PRODUCED DURING
14-DAY CONTINUOUS EXPOSURE
TO NITROGEN DIOXIDE - 38.8 mg/M^3
(NO. DEATHS/NO. EXPOSED)

TOTAL PRESSURE (mm Hg)	700	260	260	720
pO_2 (mm Hg)	140	175	260	260
GAS SUPPLY	Air	68% O_2- 32% N_2	100% O_2	36% O_2- 64% N_2
SPECIES				
MICE	2/40	8/40	0/40	-
RATS	7/50	1/50	3/50	-
DOGS	0/5	0/8	0/8	1/8
MONKEYS	4/4	3/4	2/4	4/4

TABLE V
MORTALITY PRODUCED DURING CONTINUOUS EXPOSURE TO HIGH CONCENTRATIONS OF NITROGEN DIOXIDE - 85 mg/M^3

	OCCURRENCE OF DEATHS BY SPECIES								
	MICE (40)			RATS (50)			BEAGLES (8)		
TOTAL PRESSURE (mm Hg)	260	700	720	260	700	720	260	700	720
pO_2 (mm Hg)	260	140	260	260	140	260	260	140	260
GAS SUPPLY	100% O_2	Air	36% O_2 - 64% N_2	100% O_2	Air	36% O_2 - 64% N_2	100% O_2	Air	36% O_2 - 64% N_2
DAY OF EXPOSURE									
1	0	0	0	0	41	0	0	7	0
2	9	3	3	8	9	25	2	1	7
3	8	21	15	7		18	2		0
4	2	16	2	6		3	0		0
5	1		3	1		0	2		0
6	6		*	1		*	0		*
7	4			2			0		
8	1			2			1		
9	2			4			0		
10	2			1			0		
11	3			1			0		
12	1			1			0		
13	0			1			0		
14	1			2			0		
TOTALS	40	40	23*	37	50	46*	7	8	7*

*Experiment Terminated

SECTION IV

DISCUSSION

Differences in time of onset and severity of toxic responses in animals to O_3 and NO_2 have been demonstrated between an ambient environment and reduced pressure environments containing higher than ambient partial pressures of O_2. There was a reduction in the toxicity of O_3 in the 5 psia mixed-gas environment which was even further reduced in a 5 psia-100% O_2 environment. This reduction in toxicity was indicated to be a result of the increased partial pressure of O_2, because experiments conducted at ambient pressure with a pO_2 of 260 mm Hg and at the same O_3 chamber concentration resulted in an even greater reduction in toxic response.

While a beneficial protective effect of increased O_2 partial pressure against O_3 toxicity has been demonstrated, this protective effect has only been shown to hold at a pO_2 of 260 mm Hg. Higher O_2 concentrations may not be protective, as shown by Mittler (Reference 11), and, in fact, may be synergistic in action. Indeed, O_2 itself has been shown to be toxic at partial pressures above 600 mm Hg (Reference 12).

A protective action of O_2 against NO_2 toxicity has not been clearly shown although its presence appears to prolong the life of animals exposed to lethal concentrations. There was, however, a reduction of mortality response in both mixed-gas and 100% O_2 reduced pressure (5 psia) environments compared to ambient pressure conditions.

Fairchild (Reference 13 and 14) has reported that the probable mechanism of O_3 toxicity is an action of free radicals upon biologic sulfhydryl-containing compounds of the protein-lipid lung-film layer. Stokinger (Reference 15) has stated that the mechanism of NO_2 toxicity appeared to be the same as that of O_3 by analogy of their common effects in experimental animals. It would appear from the results of the experiments described herein that there are at least subtle differences between the biologic mechanisms of action of O_3 and NO_2 that are yet to be resolved.

APPENDIX

ANIMAL EXPOSURE DATA

TABLE VI

List of Units for Hematology and Clinical Chemistry Determinations

Determinations	Units
Hematocrit (HCT)	Vol %
Hemoglobin (HGB)	g %
Red Blood Cell Count (RBC)	x 10^6
White Blood Cell Count (WBC)	x 10^3
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Total Protein (T. Prot.)	g %
Albumin (ALB.)	g %
Serum Glutamic Pyruvic Transaminase (SGPT)	Units/ml
Serum Glutamic Oxaloacetic Transaminase (SGOT)	Units/ml
Alkaline Phosphatase (Alk. Phos.)	Units/ml
Total Phosphorus (T. Phos.)	mg %
Serum Lactic Dehydrogenase (LDH)	Units/ml

TABLE VII

Experimental Conditions

Expt. No.	Contaminant and Conc. (mg/M^3)	Total Pressure (mm Hg)	pO_2 (mm Hg)
109	O_3 8	260	260
112	C*	260	260
122	O_3 8 (7.9)	700 air	
125	C	700 air	
147	O_3 8.3	260	175
150	C	Amb. air	
161	O_3 8	720	260
162	C	Amb. air	
169	O_3 8	700	260
170	C	Amb. air	
172	D.C.	700	260
173	C	Amb. air	
107	NO_2 38	260	260
108	C	260	260
123	NO_2 38	700 air	
125	C	700 air	
153	NO_2 38	260	175
154	C	Amb. air	
163	NO_2 38	720	260
164	C	Amb. air	

*C denotes Controls; D.C. denotes Dome Controls.

TABLE VIII
Mean Blood Values of Beagle Dogs Exposed to 38 mg/M^3
Nitrogen Dioxide and their Controls
Mean Values ($\pm$ Standard Deviation)

Dog Exposure Conditons - 38 mg/M^3 NO_2 - pO_2 260 mm Hg

Determinations	Expt No. 108 Control Group		Expt. No. 107 Exposure Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	48 (6)	39 (4)	43 (6)	42 (6)
HGB	15. 6 (1. 6)	13. 0 (1. 6)	15. 1 (2. 3)	13. 6 (1. 6)
RBC	3. 91 (1. 36)	6. 35 (0. 67)	4. 17 (1. 04)	3. 64 (1. 20)
WBC	14. 9 (3. 9)	15. 9 (2. 4)	13. 3 (2. 4)	12. 3 (2. 5)
Na	147 (3)	150 (4)	149 (3)	146 (3)
K	4. 8 (0. 3)	4. 3 (0. 3)	4. 9 (0. 3)	4. 4 (0. 3)
Ca	5. 4 (0. 2)	5. 1 (0. 1)	5. 4 (0. 2)	5. 3 (0. 1)
T. Prot.	5. 7 (0. 3)	5. 3 (0. 4)	5. 9 (0. 7)	5. 6 (0. 3)
Alb.	3. 4 (0. 3)	3. 1 (0. 3)	3. 5 (0. 3)	3. 4 (0. 3)
SGPT	18 (10)	28 (3)	12 (6)	28 (4)
SGOT	22 (3)	29 (3)	21 (7)	33 (2)
Alk. Phos.	2. 0 (0. 9)	3. 0 (2. 0)	3. 0 (2. 4)	3. 6 (3. 1)
T. Phos.	6. 0 (0. 9)	5. 5 (0. 4)	6. 0 (0. 5)	5. 5 (0. 6)
LDH	251 (93)	180 (0)*	332 (218)	230 (38)

* No range, identical values.

TABLE IX
Mean Blood Values of Monkeys Exposed to 38 mg/M^3
Nitrogen Dioxide and their Controls
Mean Values ($\pm$ Standard Deviation)

Monkey Exposure Conditions - 38 mg/M^3 NO_2 - pO_2 260 mm Hg

Determinations	Expt No. 108 Control Group		Expt. No. 107 Exposure Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	40 (4)	38 (3)	40 (3)	40 (2)
HGB	14.4 (2.1)	11.4 (0.5)	14.3 (2.0)	11.7 (0.9)
RBC	4.11 (1.09)	5.70 (0.40)	4.63 (0.54)	3.08 (0.17)
WBC	11.4 (3.9)	13.1 (1.6)	13.3 (3.4)	12.7 (0.5)
Na	147 (6)	147 (1)	148 (6)	145 (6)
K	4.6 (0.5)	4.5 (0.5)	5.1 (0.7)	5.1 (0.6)
Ca	5.4 (0.3)	5.3 (0.1)	5.5 (0.4)	5.6 (0.4)
T. Prot.	7.3 (0.7)	7.1 (0.5)	8.0 (0.7)	7.4 (1.2)
Alb.	4.5 (0.4)	4.7 (0.3)	4.3 (0.5)	4.0 (1.1)
SGPT	24 (9)	35 (3)	21 (8)	32 (5)
SGOT	35 (9)	58 (13)	34 (16)	43 (4)
Alk. Phos.	24.0 (4.1)	26.6 (8.8)	21.9 (6.0)	15.0 (7.8)
T. Phos.	5.7 (1.5)	7.7 (1.0)	6.8 (0.6)	6.2 (0.5)
LDH	521 (171)	555 (169)	522 (237)	480 (57)

TABLE X

Mean Blood Values of Beagle Dogs Exposed to 8.0 mg/M^3 Ozone and their Controls

Mean Values ($\pm$ Standard Deviation)

Dog — Exposure Conditions - 8.0 mg/M^3 O_3 - pO_2 260 mm Hg

Determinations	Expt No. 112 Control Group		Expt. No. 109 Exposure Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	43 (4)	39 (5)	45 (4)	43 (4)
HGB	14.0 (1.3)	12.9 (1.8)	14.5 (1.2)	14.0 (1.1)
RBC	4.54 (0.80)	4.17 (0.49)	4.92 (0.86)	4.20 (0.40)
WBC	15.8 (3.0)	14.1 (2.3)	13.4 (3.1)	18.5 (4.2)
Na	148 (4)	147 (2)	147 (4)	145 (3)
K	5.0 (0.4)	4.8 (0.3)	5.0 (0.4)	4.8 (0.3)
Ca	5.4 (0.4)	5.2 (0.1)	5.2 (0.4)	4.8 (0.2)
T. Prot.	5.6 (0.5)	6.2 (0.6)	5.6 (0.4)	5.4 (0.4)
Alb.	3.2 (0.3)	3.2 (0.4)	2.9 (1.8)	2.7 (0.2)
SGPT	21 (6)	31 (3)	20 (9)	25 (8)
SGOT	27 (7)	37 (7)	25 (7)	29 (7)
Alk. Phos.	2.8 (1.6)	2.9 (1.6)	3.7 (2.0)	4.6 (3.5)
T. Phos.	6.0 (0.9)	6.1 (0.9)	6.4 (1.0)	4.8 (1.0)
LDH	231 (106)	365 (133)	222 (88)	300 (105)

TABLE XI
Mean Blood Values of Monkeys Exposed to 8.0 mg/M^3
Ozone and their Controls
Mean Values ($\pm$ Standard Deviation)

Monkey Exposure Conditions - 8.0 mg/M^3 O_3 - pO_2 260 mm Hg

Determinations	Expt No. 112 Control Group		Expt. No. 109 Exposure Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	38 (2)	35*(2)	41 (3)	40 (3)
HGB	11.7 (0.6)	10.2 (0.3)	12.2 (0.6)	11.6 (0.8)
RBC	4.16 (0.57)	3.65 (0.13)	4.48 (0.63)	4.17 (0.29)
WBC	10.6 (1.5)	11.7 (2.3)	10.7 (2.2)	13.6 (4.5)
Na	149 (4)	148 (2)	149 (4)	146 (2)
K	4.5 (0.3)	4.1 (0.3)	4.8 (0.5)	5.2 (0.4)
Ca	5.2 (0.3)	5.3 (0.1)	5.2 (0.5)	5.0 (0.2)
T. Prot.	6.8 (0.4)	7.2 (0.3)	7.1 (0.5)	6.7 (0.5)
Alb.	4.3 (0.3)	4.2 (0.3)	4.5 (0.3)	4.4 (0.3)
SGPT	27 (4)	30 (2)	28 (3)	27 (9)
SGOT	40 (11)	34 (11)	37 (12)	45 (7)
Alk. Phos.	26.9 (7.1)	22.8 (7.8)	27.8 (10.8)	22.6 (9.6)
T. Phos.	5.7 (0.6)	5.6 (0.7)	5.9 (1.1)	6.3 (0.8)
LDH	498 (259)	580 (208)	420 (166)	728 (170)

TABLE XII
Mean Blood Values of Beagle Dogs Exposed to 36 mg/M^3
Nitrogen Dioxide and their Controls
Mean Values ($\pm$ Standard Deviation)

Dog   Exposure Conditions - 36 mg/M^3 NO_2 - pO_2 140 mm Hg

Determinations	Expt No. 125 Control Group		Expt. No. 123 Exposure Group	
	Period		Period	
	Baseline	Exptl *	Baseline	Exptl
HCT	46 (1)	50 (0)	42 (4)	44 (3)
HGB	14.3 (1.0)	15.7 (0)	13.5 (1.0)	13.8 (0.8)
RBC	4.27 (0.25)	5.20 (0)	4.32 (0.46)	4.37 (0.38)
WBC	11.6 (2.2)	7.9 (0)	11.2 (1.8)	15.9 (2.1)
Na	146 (2)	148 (0)	146 (2)	146 (2)
K	5.2 (0.2)	5.2 (0)	5.0 (0.3)	4.9 (0.4)
Ca	5.5 (0.1)	5.6 (0)	5.7 (0.2)	5.4 (0.1)
T. Prot.	5.4 (0.2)	5.4 (0)	5.6 (0.3)	5.7 (0.2)
Alb.	3.5 (0.1)	3.6 (0)	3.4 (0.3)	3.3 (0.2)
SGPT	23 (6)	22 (0)	31 (12)	29 (4)
SGOT	26 (5)	26 (0)	36 (11)	39 (7)
Alk. Phos.	4.0 (0.6)	3.8 (0)	1.9 (0.8)	1.9 (0.8)
T. Phos.	6.4 (0.6)	5.9 (0)	6.6 (0.7)	6.2 (0.6)
LDH	170 (55)	180 (0)	150 (109)	90 (31)

* No range, single survivor.

TABLE XIII
Mean Blood Values of Monkeys Exposed to 7.9 mg/M^3
Ozone and their Controls
Mean Values (± Standard Deviation)

Monkey — Exposure Conditions - 7.9 mg/M^3 O_3 - pO_2 140 mm Hg

Determinations	Expt No. 125 Control Group		Expt. No. 122 Exposure Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	39 (2)	39 (3)	40 (2)	40 (1)
HGB	11.6 (0.7)	11.9 (1.2)	12.0 (0.5)	12.2 (0.7)
RBC	4.31 (0.39)	4.50 (0.32)	4.34 (0.33)	4.12 (0.42)
WBC	12.9 (1.7)	15.1 (2.1)	11.1 (3.0)	8.6 (0.1)
Na	148 (3)	149 (1)	151 (3)	145 (1)
K	4.6 (1.0)	4.7 (0.5)	5.2 (1.0)	6.0 (1.1)
Ca	5.6 (0.2)	5.5 (0.2)	5.8 (0.2)	5.9 (0.1)
T. Prot.	7.1 (0.3)	6.8 (0.6)	7.3 (0.5)	7.2 (0.2)
Alb.	4.5 (0.4)	4.2 (0.3)	4.7 (0.4)	4.1 (0.5)
SGPT	36 (14)	33 (5)	32 (7)	24 (2)
SGOT	49 (9)	44 (5)	51 (18)	60 (35)
Alk. Phos.	23.3 (13.2)	19.9 (11.0)	31.1 (4.9)	22.8 (5.3)
T. Phos.	5.9 (1.5)	6.4 (2.0)	6.1 (1.5)	5.2 (0.3)
LDH	468 (249)	375 (79)	360 (174)	600 (167)

TABLE XIV
Mean Blood Values of Beagle Dogs Exposed to 8.3 mg/M^3
Ozone and their Controls
Mean Values ($\pm$ Standard Deviation)

Dog — Exposure Conditions - 8.3 mg/M^3 O_3 - pO_2 260 mm Hg

	Expt No. 150 Control Group		Expt. No. 147 Exposure Group	
	Period		Period	
Determinations	Baseline	Exptl	Baseline	Exptl
HCT	44 (3)	49 (2)	45 (4)	48 (4)
HGB	15.5 (1.1)	15.6 (0.7)	15.5 (1.2)	14.4 (1.7)
RBC	6.28 *0.39)	6.75 (0.25)	6.22 (0.50)	6.63 (0.06)
WBC	13.8 (3.2)	13.8 (2.6)	11.8 (3.1)	41.7 (2.2)
Na	143 (1)	148 (2)	143 (2)	140 (6)
K	4.5 (0.3)	5.6 (0.5)	4.8 (0.3)	4.7 (0.4)
Ca	5.5 (0.2)	5.9 (0.1)	5.5 (0.2)	5.4 (0)*
T. Prot.	5.5 (0.4)	6.0 (0.3)	5.5 (0.5)	6.2 (0.1)
Alb.	3.3 (0.2)	3.6 (0.2)	3.5 (0.8)	3.8 (1.1)
SGPT	20 (8)	21 (6)	24 (9)	12 (3)
SGOT	28 (9)	37 (6)	29 (13)	52 (17)
Alk. Phos.	2.5 (1.9)	1.8 (1.9)	3.0 (1.8)	6.5 (2.1)
T. Phos.	5.2 (0.8)	6.0 (0.4)	5.4 (1.1)	4.6 (0.5)
LDH	252 (83)	383 (170)	246 (79)	645 (516)

* No range, identical values.

TABLE XV
Mean Blood Values of Monkeys Exposed to 8.3 mg/M^3
Ozone and their Controls
Mean Values ($\pm$ Standard Deviation)

Monkey Exposure Conditions - 8.3 mg/M^3 O_3 - pO_2 260 mm Hg

	Expt No. 150 Control Group		Expt. No. 147 Exposure Group	
	Period		Period	
Determinations	Baseline	Exptl	Baseline	Exptl
HCT	39 (2)	41 (4)	40 (4)	39 (4)
HGB	12.4 (1.3)	12.0 (1.7)	12.4 (1.3)	11.1 (1.3)
RBC	5.15 (0.51	5.33 (0.82)	4.75 (1.39)	5.55 (0)*
WBC	9.2 (2.0)	13.4 (4.4)	11.7 (2.5)	10.7 (4.2)
Na	147 (3)	148 (1)	146 (4)	144 (1)
K	4.7 (0.5)	5.1 (0.1)	4.8 (0.5)	4.9 (0.4)
Ca	5.6 (0.4)	6.0 (0.4)	5.5 (0.2)	5.5 (0.3)
T. Prot.	7.4 (0.9)	7.3 (1.0)	7.3 (0.5)	6.9 (0.8)
Alb.	4.4 (0.3)	3.9 (0.3)	4.4 (0.3)	3.6 (0.4)
SGPT	30 (5)	20 (3)	38 (20)	44 (43)
SGOT	37 (6)	38 (4)	50 (12)	80 (61)
Alk. Phos.	23.5 (3.2)	18.0 (2.1)	26.8 (5.6)	13.7 (4.3)
T. Phos.	4.6 (1.1)	4.4 (0.2)	5.1 (1.1)	5.2 (0.5)
LDH	376 (135)	475 (64)	560 (39)	647 (81)

* Extremely small positive value.

TABLE XVI
Mean Blood Values of Beagle Dogs Exposed to 36.4 mg/M^3
Nitrogen Dioxide and their Controls
Mean Values ($\pm$ Standard Deviation)

Dog Exposure Conditions - 36.4 mg/M^3 NO_2 - pO_2 180 mm Hg

	Expt No. 154 Control Group		Expt. No. 153 Exposure Group	
	Period		Period	
Determinations	Baseline	Exptl	Baseline	Exptl
HCT	44 (2)	46 (2)	45 (3)	43 (3)
HGB	14.8 (1.1)	16.1 (0.8)	15.1 (1.2)	15.0 (1.0)
RBC	6.28 (0.29)	6.54 (0.40)	6.18 (0.33)	6.10 (0.30)
WBC	15.6 (2.9)	12.1 (2.4)	13.2 (2.2)	13.1 (2.4)
Na	142 (2)	145 (2)	142 (2)	145 (1)
K	4.6 (0.2)	5.1 (0.5)	4.6 (0.4)	4.7 (0.2)
Ca	5.4 (0.2)	5.6 (0.2)	5.4 (0.2)	5.7 (0.1)
T. Prot.	5.7 (0.3)	5.9 (0.4)	5.8 (0.4)	5.8 (0.3)
Alb.	3.5 (0.2)	3.7 (0.4)	3.4 (0.3)	3.1 (0.6)
SGPT	20 (6)	28 (3)	21 (8)	35 (8)
SGOT	30 (8)	40 (9)	29 (10)	45 (8)
Alk. Phos.	1.0 (0.6)	1.2 (1.7)	1.5 (0.8)	1.4 (2.2)
T. Phos.	4.8 (0.7)	5.7 (0.6)	5.3 (0.9)	5.3 (0.7)
LDH	224 (86)	330 (131)	236 (94)	193 (73)

TABLE XVII
Mean Blood Values of Monkeys Exposed to 36.4 mg/M³
Nitrogen Dioxide and their Controls
Mean Values (± Standard Deviation)

Monkey — Exposure Conditions - 36.4 mg/M³ NO_2 - pO_2 180 mm Hg

Determinations	Expt No. 154 Control Group, Period: Baseline	Expt No. 154 Control Group, Period: Exptl	Expt. No. 153 Exposure Group, Period: Baseline	Expt. No. 153 Exposure Group, Period: Exptl*
HCT	41 (2)	43 (1)	41 (3)	41 (0)
HGB	12.9 (0.7)	13.2 (0)**	12.9 (0.9)	12.8 (0)
RBC	5.18 (0.25)	5.27 (0.13)	5.48 (0.42)	5.74 (0)
WBC	11.7 (3.4)	15.5 (0.7)	12.6 (4.2)	20.2 (0)
Na	145 (4)	148 (3)	146 (3)	148 (0)
K	4.6 (0.5)	4.6 (0.5)	4.9 (0.7)	5.5 (0)
Ca	5.4 (0.3)	5.5 (0.1)	5.6 (0.3)	5.9 (0)
T. Prot.	7.2 (0.5)	7.8 (0)**	7.5 (0.5)	7.8 (0)
Alb.	4.5 (0.3)	4.7 (0.1)	4.4 (0.4)	3.7 (0)
SGPT	29 (4)	46 (6)	28 (7)	39 (0)
SGOT	43 (8)	57 (10)	42 (9)	55 (0)
Alk. Phos.	22.2 (4.1)	12.1 (1.0)	26.6 (4.7)	22.5 (0)
T. Phos.	5.5 (0.7)	5.1 (0.5)	5.3 (1.5)	4.1 (0)
LDH	553 (127)	470 (4)	435 (160)	520 (0)

* No range, single survivor.

** No range, identical values.

TABLE XVIII
Mean Blood Values of Beagle Dogs Exposed to 8.0 mg/M^3
Ozone and their Controls
Mean* Values (± Standard Deviation)

Dog Exposure Conditions - 8.0 mg/M^3 O_3 - pO_2 260 mm Hg

Determinations	Expt No. 162 Control Group — Period: Baseline	Expt No. 162 Control Group — Period: Exptl	Expt. No. 161 Exposure Group — Period: Baseline	Expt. No. 161 Exposure Group — Period: Exptl
HCT	41 (4)	44 (4)	43 (4)	43 (3)
HGB	13.4 (1.5)	14.9 (1.4)	13.9 (1.4)	14.6 (0.9)
RBC	6.09 (0.44)	6.33 (0.38)	6.07 (0.57)	6.19 (0.48)
WBC	13.3 (1.4)	12.3 (2.6)	11.9 (2.5)	20.0 (3.3)
Na	145 (4)	145 (3)	145 (2)	143 (2)
K	5.0 (0.3)	5.0 (0.5)	4.9 (0.3)	4.7 (0.2)
Ca	5.8 (0.2)	5.6 (0)*	5.6 (0.2)	5.6 (0.2)
T. Prot.	5.6 (0.3)	5.7 (0.3)	5.7 (0.3)	5.8 (0.2)
Alb.	3.4 (0.4)	3.3 (0.2)	3.4 (0.3)	3.4 (0.1)
SGPT	23 (9)	20 (3)	28 (11)	26 (14)
SGOT	29 (10)	34 (4)	27 (6)	37 (10)
Alk. Phos.	3.6 (1.8)	2.9 (1.8)	2.2 (1.4)	1.4 (0.7)
T. Phos.	6.2 (0.7)	6.3 (1.6)	5.7 (1.2)	5.3 (0.7)
LDH	193 (88)	155 (58)	189 (89)	265 (184)

* Extremely small positive value.

TABLE XIX
Mean Blood Values of Monkeys Exposed to 8.0 mg/M^3
Ozone and their Controls
Mean Values ($\pm$ Standard Deviation)

Monkey Exposure Conditions - 8.0 mg/M^3 O_3 - pO_2 260 mm Hg

Determinations	Expt No. 162 Control Group		Expt. No. 161 Exposure Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	43 (3)	43 (1)	42 (3)	38 (3)
HGB	13.3 (0.8)	13.0 (0.9)	12.6 (1.0)	12.1 (1.1)
RBC	5.49 (0.23)	5.18 (0.28)	5.41 (0.39)	5.23 (0.37)
WBC	12.4 (1.3)	14.1 (5.1)	12.7 (2.0)	13.4 (2.5)
Na	148 (3)	144 (1)	148 (3)	146 (3)
K	5.0 (0.4)	5.1 (0.4)	5.4 (1.1)	5.4 (0.3)
Ca	5.8 (0.3)	5.7 (0.2)	5.8 (0.4)	5.5 (0.2)
T. Prot.	8.0 (0.4)	7.9 (0.1)	7.7 (0.5)	7.5 (0.5)
Alb.	4.3 (0.4)	4.4 (0.3)	4.3 (0.3)	4.0 (0.3)
SGPT	23 (8)	23 (4)	26 (12)	31 (21)
SGOT	41 (9)	49 (9)	38 (13)	41 (12)
Alk. Phos.	23.8 (11.3)	20.6 (13.2)	25.6 (9.0)	22.0 (6.8)
T. Phos.	6.0 (0.8)	7.7 (1.8)	6.3 (1.7)	5.5 (1.5)
LDH	533 (177)	680 (57)	396 (159)	460 (216)

TABLE XX
Mean Blood Values of Beagle Dogs Exposed to 38 mg/M^3
Nitrogen Dioxide and their Controls
Mean Values ($\pm$ Standard Deviation)

Dog — Exposure Conditions - 38 mg/M^3 NO_2 - pO_2 260 mm Hg

Determinations	Expt No. 164 Control Group — Period: Baseline	Expt No. 164 Control Group — Period: Exptl	Expt. No. 163 Exposure Group — Period: Baseline	Expt. No. 163 Exposure Group — Period: Exptl
HCT	45 (3)	48 (4)	43 (4)	41 (2)
HGB	15. 2 (1. 2)	16. 6 (1. 0)	14. 3 (1. 4)	14. 1 (0. 8)
RBC	6. 42 (0. 42)	6. 61 (0. 48)	6. 14 (0. 42)	5. 60 (0. 33)
WBC	13. 5 (2. 3)	15. 2 (1. 3)	14. 8 (2. 5)	16. 5 (4. 0)
Na	145 (3)	142 (1)	145 (3)	141 (2)
K	5. 2 (0. 4)	5. 0 (0. 2)	4. 9 (0. 3)	4. 8 (0. 3)
Ca	5. 7 (0. 2)	5. 8 (0. 1)	5. 7 (0. 2)	5. 7 (0. 1)
T. Prot.	6. 0 (0. 3)	5. 7 (0. 4)	6. 1 (0. 4)	6. 0 (0. 4)
Alb.	3. 4 (0. 1)	3. 5 (0)*	3. 4 (0. 2)	3. 1 (0. 2)
SGPT	21 (5)	20 (12)	18 (5)	23 (3)
SGOT	28 (8)	25 (2)	26 (7)	28 (6)
Alk. Phos.	2. 2 (1. 0)	1. 2 (0. 7)	1. 6 (1. 0)	1. 2 (0. 6)
T. Phos.	5. 9 (1. 3)	5. 3 (1. 7)	5. 7 (0. 8)	5. 1 (0. 7)
LDH	209 (109)	190 (220)	210 (128)	251 (222)

* Extremely small positive value.

TABLE XXI
Mean Blood Values of Beagle Dogs Exposed to 8.0 mg/M^3
Ozone and their Controls
Mean Values (± Standard Deviation)

Dog Exposure Conditions - 8.0 mg/M^3 O_3 - pO_2 260 mm Hg

Determinations	Expt No. ___ Control Group		Expt. No. ___ Exposure Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	44 (3)	44 (3)	43 (3)	44 (3)
HGB	14.6 (1.1)	14.6 (1.2)	14.2 (1.2)	14.5 (1.1)
RBC	6.18 (0.36)	5.94 (0.36)	6.07 (0.41)	6.10 (0.44)
WBC	13.8 (2.9)	11.9 (2.7)	12.9 (1.6)	21.9 (1.2)
Na	145 (3)	143 (1)	144 (3)	146 (3)
K	5.0 (0.3)	4.9 (0.4)	4.9 (0.3)	5.2 (0.3)
Ca	5.6 (0.2)	6.0 (0.1)	5.7 (0.2)	5.7 (0.1)
T. Prot.	6.2 (0.4)	5.9 (0.2)	5.9 (0.2)	6.0 (0.3)
Alb.	3.4 (0.2)	3.2 (0.2)	3.4 (0.3)	3.4 (0.1)
SGPT	20 (9)	31 (9)	22 (10)	35 (3)
SGOT	24 (9)	34 (7)	24 (10)	29 (12)
Alk. Phos.	1.3 (0.9)	1.3 (1.0)	1.0 (0.6)	1.8 (0.7)
T. Phos.	5.0 (0.7)	5.4 (0.9)	5.1 (0.7)	4.1 (2.6)
LDH	198 (82)	235 (90)	253 (139)	290 (25)

TABLE XXII
Mean Blood Values of Monkeys Exposed to 8.0 mg/M^3
Ozone and their Controls
Mean Values ($\pm$ Standard Deviation)

Monkey Exposure Conditions - 8.0 mg/M^3 O_3 - pO_2 260 mm Hg

Determinations	Expt No. 170 Control Group		Expt. No. 169 Exposure Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	40 (2)	44 (4)	39 (2)	38 (4)
HGB	12. 2 (0.7)	13.0 (0.9)	12.0 (1.0)	11.8 (1.0)
RBC	5.10 (0.30)	5.31 (0.77)	5.15 (0.32)	5.02 (0.33)
WBC	13.4 (3.5)	12.0 (4.2)	13.5 (3.3)	14.8 (0.9)
Na	145 (2)	143 (4)	145 (3)	147 (3)
K	5.0 (0.6)	4.3 (0.4)	4.8 (0.4)	5.7 (1.7)
Ca	5.6 (0.2)	5.7 (0.5)	5.8 (0.2)	5.7 (0.2)
T. Prot.	7.3 (0.9)	8.0 (0.4)	7.3 (0.5)	7.7 (0.2)
Alb.	4.0 (0.2)	4.6 (0.6)	4.2 (0.3)	4.1 (0.1)
SGPT	36 (9)	76 (63)	31 (7)	39 (14)
SGOT	42 (11)	40 (19)	45 (10)	44 (12)
Alk. Phos.	24.0 (12.5)	20.2 (4.6)	21.8 (6.7)	20.2 (5.0)
T. Phos.	6.0 (0.9)	7.2 (4.7)	5.8 (0.8)	7.2 (1.3)
LDH	760 (353)	615 (190)	584 (219)	770 (84)

TABLE XXIII
Mean Blood Values of Chamber and Animal Room Control
Beagle Dogs
Mean Values (± Standard Deviation)

Determinations	Expt No. 173 Animal Room Control Group		Expt. No. 172 Chamber Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT	42 (3)	44 (1)	44 (3)	43 (3)
HGB	13.9 (1.1)	15.0 (0.8)	14.9 (1.2)	14.7 (1.0)
RBC	5.88 (0.45)	6.33 (0.52)	6.26 (0.38)	6.15 (0.41)
WBC	11.6 (.24)	13.6 (2.6)	13.4 (3.9)	14.0 (2.4)
Na	144 (3)	141 (2)	142 (2)	143 (3)
K	4.9 (0.3)	5.3 (0.3)	4.8 (0.3)	4.8 (0.2)
Ca	5.6 (0.2)	5.9 (0.1)	5.6 (0.2)	5.6 (0.1)
T. Prot.	5.8 (0.4)	5.7 (0.4)	6.0 (1.6)	6.2 (0.3)
Alb.	3.3 (0.2)	3.2 (0.2)	3.3 (0.2)	3.2 (0.1)
SGPT	30 (5)	26 (5)	32 (4)	34 (3)
SGOT	34 (8)	34 (2)	37 (4)	41 (6)
Alk. Phos.	2.2 (1.3)	1.7 (1.1)	1.5 (1.4)	0.9 (0.7)
T. Phos.	5.3 (1.1)	5.7 (1.0)	5.2 (1.1)	5.3 (1.1)
LDH	392 (177)	235 (57)	318 (133)	268 (91)

TABLE XXIV
Mean Blood Values of Chamber and Animal Room Control Monkeys
Mean Values (± Standard Deviation)

Determinations	Expt No. 173 Animal Room Control Group — Period: Baseline	Expt No. 173 Animal Room Control Group — Period: Exptl	Expt. No. 172 Chamber Group — Period: Baseline	Expt. No. 172 Chamber Group — Period: Exptl
HCT	41 (1)	43 (3)	39 (2)	38 (2)
HGB	12.6 (0.8)	12.8 (1.1)	11.5 (0.6)	11.3 (0.5)
RBC	5.39 (0.15)	5.66 (0.11)	5.29 (0.33)	5.12 (0.28)
WBC	12.9 (3.2)	14.5 (1.8)	16.4 (4.8)	11.8 (2.1)
Na	144 (3)	142 (3)	144 (3)	141 (1)
K	5.2 (0.7)	4.4 (1.3)	5.2 (0.7)	5.0 (0.4)
Ca	5.8 (0.4)	5.7 (0.7)	5.8 (0.4)	5.6 (0.2)
T. Prot.	2.5 (0.1)	7.7 (0.2)	7.6 (0.4)	7.7 (0.2)
Alb.	4.1 (0.4)	4.5 (0.5)	4.0 (0.4)	4.5 (0.2)
SGPT	32 (7)	27 (2)	31 (6)	29 (3)
SGOT	48 (14)	48 (4)	52 (8)	61 (11)
Alk. Phos.	9.8 (3.3)	13.5 (5.7)	31.9 (16.5)	24.6 (12.7)
T. Phos.	5.8 (0.6)	5.8 (0.3)	5.7 (2.1)	6.3 (0.9)
LDH	706 (233)	390 (71)	837 (211)	775 (323)

TABLE XXV
Mean Blood Values of Chamber and Animal Room Control
Rats (Male)
Mean Values (± Standard Deviation)

Determinations	Expt No. 173 Animal Room Control Group, Period: Baseline	Expt No. 173 Animal Room Control Group, Period: Exptl	Expt. No. 172 Chamber Group, Period: Baseline	Expt. No. 172 Chamber Group, Period: Exptl
HCT		38 (5)		45 (6)
HGB		12.9 (1.6)		11.6 (1.1)
RBC		6.41 (0.40)		5.32 (0.67)
WBC		11.5 (5.6)		6.2 (2.1)
Na		142 (3)		144 (4)
K		5.6 (0.1)		5.1 (0.4)
Ca		5.5 (0.1)		5.8 (0.3)
T. Prot.		6.3 (0.1)		6.9 (0.1)
Alb.		3.4 (0.2)		4.1 (0.3)
SGPT		34 (6)		39 (4)
SGOT		108 (13)		129 (16)
Alk. Phos.		25.7 (11.9)		20.5 (7.7)
T. Phos.		7.4 (0.5)		6.2 (0.4)
LDH		1200 (160)		2320 (240)

TABLE XXVI
Mean Blood Values of Chamber and Animal Room Control
Rats (Female)
Mean Values (± Standard Deviation)

Determinations	Expt No. 173 Animal Room Control Group		Expt. No. 172 Chamber Group	
	Period		Period	
	Baseline	Exptl	Baseline	Exptl
HCT		41 (3)		40 (5)
HGB		12.8 (1.4)		12.6 (1.9)
RBC		6.15 (0.42)		6.25 (0.62)
WBC		6.4 (1.0)		8.3 (2.1)
Na		140 (1)		149 (5)
K		5.5 (0.5)		5.0 (0.5)
Ca		5.6 (0.1)		6.2 (0.5)
T. Prot.		6.2 (0.2)		6.5 (0.1)
Alb.		3.3 (0.1)		3.8 (0.1)
SGPT		37 (8)		44 (6)
SGOT		126 (16)		129 (16)
Alk. Phos.		68.0 (8.5)		41.1 (13.3)
T. Phos.		9.4 (0.5)		6.2 (1.0)
LDH		1487 (415)		1667 (393)

REFERENCES

1. Sandage, C. Tolerance Criteria for Continuous Inhalation Exposure to Toxic Material I. Effects on Animals of 90-Day Exposure to Phenol, CCl_4, and a Mixture of Indole, Skatole, H_2S and Methyl Mercaptan, ASD Technical Report, 61-519(I), AD 268783, Aerospace Medical Research Laboratories, October, 1961.

2. Sandage, C. Tolerance Criteria for Continuous Inhalation Exposure to Toxic Material II. Effects on Animals of 90-Day Exposure to H_2, Methyl Mercaptan, Indole, and a Mixture of H_2S, Methyl Mercaptan, Indole, and Skatole, ASD Technical Report 61-519(II), AD 287797, Aerospace Medical Research Laboratories, December, 1961.

3. House, W. B. Tolerance Criteria for Continuous Inhalation Exposure to Toxic Materials III. Effects on Animals of 90-Day Exposure to Hydrazine, Unsymmetrical Dimethylhydrazine (UDMH), Decaborane, and Nitrogen Dioxide, ASD Technical Report 61-519(III), AD 44025L, Aerospace Medical Research Laboratories, February, 1964.

4. Hargreaves, J. J., W. G. Robertson, F. Ulvedal, H. J. Zeft, and B. E. Welch. "The Study of Man During a 56-Day Exposure to an Oxygen-Helium Atmosphere at 258 mm Hg Total Pressure: I. Introduction and General Experimental Design," Aerospace Med., 37, 552, 1966.

5. Adams, J. D., J. P. Conkle, W. E. Mabson, J. T. Watson, P. H. Wolf, and B. E. Welch. "The Study of Man During a 56-Day Exposure to an Oxygen-Helium Atmosphere at 258 mm Hg Total Pressure: II. Major and Minor Atmospheric Components," Aerospace Med., 37, 555, 1966.

6. McNerney, J. M. and J. D. MacEwen. "Comparative Toxicity Studies at Reduced and Ambient Pressures, I. Acute Response," Am. Ind. Hyg. J., 26:568-573, 1965.

7. MacEwen, J. D. Toxic Hazards Research Unit Design and Construction Phase, AMRL-TR-65-125, AD 624473, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, September, 1965.

8. Byers, D. H., and B. E. Saltzman. "Determination of Ozone in Air by Neutral and Alkaline Iodide Procedures," Amer. Ind. Hyg. Assoc. J., 19:251, 1958.

9. Saltzman, B. E. "Colorimetric Microdetermination of Nitrogen Dioxide in the Atmosphere," Anal. Chem., 26:1949, 1954.

10. McNerney, J. M. "Preliminary Results of Toxicity Studies at 5 psia, 100% Oxygen Environment," Proceedings of the Conference on Atmospheric Contamination in Confined Spaces, AMRL-TR-65-230, AD 629622, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, December, 1965.

11. Mittler, S. "Toxicity of Ozone IV, Silicone Aerosols and Alcohol Vapor Therapy in Ozone Poisoning," Ind. Med. and Surg., 27:43, 1958.

12. MacEwen, J. D. and C. C. Haun. "Oxygen Toxicity at Near Ambient Pressures," Proceedings of the 2nd Annual Conference on Atmospheric Contamination in Confined Spaces, AMRL-TR-66-120, AD 646512, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, December, 1966.

13. Fairchild, E. J. II. "Neurohumoral Factors in Injury From Inhaled Irritants, Arch. Envir. Health, 6:79, 1963.

14. Fairchild, E. J. II. and S. L. Graham. "Thyroid Influence on the Toxicity of Respiratory Irritant Gases, Ozone and Nitrogen Dioxide," J. Pharmacol. Exptl. Therap. 139, 177, 1963.

15. Handbook of Physiology, Vol. II of Section III. W. O. Fenn and H. Rhan (editors), Chapter 42, American Physiology Society, Washington, D.C., 1965.

Security Classification

DOCUMENT CONTROL DATA - R&D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1. ORIGINATING ACTIVITY (Corporate author) Aerojet-General Corporation Dayton, Ohio 45431	2a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED 2b. GROUP N/A

3. REPORT TITLE

THE EFFECT OF A MIXED GAS ATMOSPHERE AT 5 PSIA ON THE INHALATION TOXICITY OF O_3 & NO_2

4. DESCRIPTIVE NOTES (Type of report and inclusive dates)

Final Report, October 1964 - July 1966

5. AUTHOR(S) (Last name, first name, initial)

J.D. MacEwen R.P. Geckler
C.C. Haun J.M. McNerney

6. REPORT DATE	7a. TOTAL NO. OF PAGES	7b. NO. OF REFS
December 1967	36	15

8a. CONTRACT OR GRANT NO. AF 33(657)-11305 b. PROJECT NO. 6302 c. Task No. 630201 d.	9a. ORIGINATOR'S REPORT NUMBER(S) Aerojet-General Corp. No. 3267 9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report) AMRL-TR-67-69

10. AVAILABILITY/LIMITATION NOTICES

Distribution of this document is unlimited. It may be released to the Clearinghouse, Department of Commerce, for sale to the general public.

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A mixed gas atmosphere (68% O_2-32% N_2) at 5 psia pressure was shown to reduce the acute toxic effect of ozone (O_3) in animals when compared with an identical O_3 concentration under ambient pressure conditions. The actual reduction of O_3 toxicity in the 5 psia-mixed gas environment was not as great as that seen in a 5 psia-100% O_2 environment. Further experimentation with increased O_2 partial pressures at ambient total pressures led to the conclusion that an increased pO_2 of 260 mm Hg was protective against acute O_3 effects. No significant differences were seen between 5 psia-mixed gas and 5 psia-100% O_2 environments on the effect of nitrogen dioxide (NO_2) toxicity in animals although both provide some apparent protection compared with ambient pressure conditions.

DD FORM 1 JAN 64 1473

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14. KEY WORDS	LINK A		LINK B		LINK C	
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Space Cabin Toxicology						
Oxygen						
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